

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 December 2003 (24.12.2003)

PCT

(10) International Publication Number
WO 2003/105770 A3

(51) International Patent Classification⁷: **C07D 473/00**,
473/02, 473/04, 473/16, 473/18, 473/20, 473/22, 473/24,
473/26, 473/28, 473/30, 473/32, 473/34, 473/36, 473/38,
473/40, A61K 31/52, 31/522, A61P 31/14

(21) International Application Number:
PCT/US2003/018841

(22) International Filing Date: 14 June 2003 (14.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/389,161 17 June 2002 (17.06.2002) US

(71) Applicants (for all designated States except US): **MERCK & CO., INC.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **ISIS PHARMACEUTICALS, INC.** [US/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BHAT, Balkrishen** [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **BHAT, Neelima** [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **DANDE, Prasad** [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **ELDRUP, Anne, B.** [DK/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **OLSEN, David, B.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **MACCOSS, Malcolm** [GB/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(74) Common Representative: **MERCK & CO., INC.**; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
7 October 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CARBOCYCLIC NUCLEOSIDE ANALOGS AS RNA-ANTIVIRALS

(57) Abstract: The present invention provides carbocyclic nucleoside compounds and certain derivatives thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compounds are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compositions containing such carbocyclic nucleoside compounds alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the carbocyclic nucleoside compounds of the present invention



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/18841

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07D 473/00, 473/02, 473/04, 473/16, 473/18, 473/20, 473/22, 473/24, 473/26, 473/28, 473/30 473/32, 473/34, 473/36, 473/38, 473/40; A61K 31/52; 31/522; A61P 31/14
US CL : 544/224, 264, 265, 266, 271, 272, 276, 277, 280, 311, 314, 316, 317, 318 514/81, 263.3, 263.34, 263.37, 263.4
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : Please See Continuation Sheet

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS online

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- A	ROSENQUIST et al. Synthesis of Carbocyclic 2',3'-Dideoxy-2'-C-hydroxymethyl Nucleosides as Potential Inhibitors of HIV. J. Org. Chem. 1994, Vol. 59, pages 1779-1782, see 2 and 11 and 12.	1-2, 12, 13, 18, 20 ----- 3, 4, 7, 8, 14-17, 19, 21
X --- A	CAAMANO et al. Synthesis and evaluation of antiviral activity of higher homologs of xylo-carbocyclic nucleosides. Nucleosides, Nucleotides & Nucleic Acids. 2001, Vol. 20, No. 4-7, pages 1137-1139, see the tremethanol species with hypoxanthine, 6-Cl-purine and adenine 6, 3a and 3b.	1-2, 12, 13, 18, 20 ----- 3, 4, 7, 8, 14-17, 19-21
Y --- A	US 5,473,063 A (CLASSON et al) 05 December 1995, see Formula 1Ab and example 17.	1, 2, 12, 13, 18, 20 ----- 3, 4, 7, 8, 14-17, 19-21
X --- A	US 5,409,906 A (DATEMA ^{et al.}) 25 April 1995, see compounds 11, 17, 14, 20.	1, 12, 13, 18, 20, 14-17, 19, 21
A	US 5,723,466 A (BORCHERDING ^{et al.}) 03 March 1998, see entire document.	1-21

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	"T"
"A" document defining the general state of the art which is not considered to be of particular relevance	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

30 April 2004 (30.04.2004)

Date of mailing of the international search report

26 JUL 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Mark L. Berch

Telephone No. 571-272-0663

INTERNATIONAL SEARCH REPORT

International application N .

PCT/US03/18841

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☒

The additional search fees were accompanied by the applicant's protest.

N protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/18841

Continuation of Item 4 of the first sheet:

Title Too Long. New Title: "CABOCYCLIC NUCLEOSIDE ANALOGS AS RNA ANTIVIRALS".

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I , claim(s) 1(part), 12-21(part) drawn to Pyrimidines.

Group II , claim(s) 1(part), 2(part), 3-4, 7-8, 11(part), 12-21(part), drawn to Purines.

Group III , claim(s) 1(part), 2(part), 5-6, 9-10, 11(part), 12-21(part), drawn to Pyrrolopyrimidines.

The inventions listed as Groups I -III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: each group has the special technical feature of a different heterocyclic core. These have marked structural differences. Group I is unfused; Group II has 4 heteroatoms, Group III has only three.

Continuation of B. FIELDS SEARCHED Item 1:

544/224, 264, 265, 266, 271, 272, 276, 277, 280, 311, 314, 316, 317, 318;
514/81, 263.3, 263.34, 263.37, 263.4